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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No. 6,753,147 ) Serial No. 09/981,356  
Inventor(s): Bert VOGELSTEIN *et al* ) Filed: October 12, 2001  
Issue Date: June 22, 2004 ) Attorney Docket No. 001107.00195  
For: DIGITAL AMPLIFICATION

**REQUEST FOR CERTIFICATE OF CORRECTION**

U.S. Patent and Trademark Office  
Customer Service Window  
Randolph Building, Mail Stop: Certificate of Correction Branch  
401 Dulany Street  
Alexandria, VA 22314

Sir:

Pursuant to 35 U.S.C. § 254 and 37 C.F.R. § 1.322, this is a request for the issuance of a Certificate of Correction in the above-identified patent. Two (2) copies of PTO Form 1050 are appended. The complete Certificate of Correction involves one page.

The mistakes identified in the appended Form occurred through no fault of the Applicants, as clearly disclosed by the records of the application, which matured into this patent. Enclosed for your convenience are the relevant portions of the Amendment filed January 8, 2004.

Issuance of the Certificate of Correction containing the corrections is respectfully requested. Since these changes are necessitated through no fault of the Applicants, no fee is believed to be associated with this request. Nonetheless, should the Patent and Trademark Office determine that a fee is required, please charge our Deposit Account No. 19-0733.

Respectfully submitted,

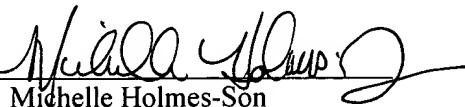
BANNER & WITCOFF, LTD.

Dated:

April 8, 2005

1001 G Street, N.W. (11th Fl.)  
Washington, D.C. 20001  
(202) 824-3000

By:



Michelle Holmes-Son  
Registration No. 47,660

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO.: 6,753,147  
DATED: June 22, 2004  
INVENTOR(S): Bert VOGELSTEIN *et al*

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Column 17, Claim 4, Line 17:  
Please delete "second"

In Column 18, Claim 7, Line 5:  
Please delete "comprising"

In Column 18, Claim 9, Line 42:  
Please delete "first"

Mailing Address of Sender:

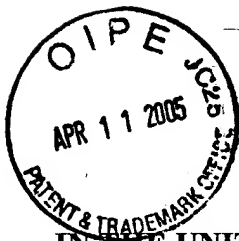
Banner & Witcoff, Ltd.  
11th Floor  
1001 G Street, N.W.  
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U.S. PAT. NO 6,753,147

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BMW R100 507



PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

*In re* Application of: )  
Bert Vogelstein *et al.* ) Group Art Unit: 1637  
Serial No.: 09/981,356 ) Examiner: J. Siew  
Filed: October 12, 2001 ) Atty. Docket No.: 001107.00195

For: DIGITAL AMPLIFICATION

**SECOND AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In response to the Advisory Action mailed December 24, 2003, and the final Office Action mailed August 28, 2003, applicants request entry of the following amendments and reconsideration of the patentability of the rejected claims. Claims 65-68, 70-103, and 109-116 were pending in the application and stand rejected.

A petition for a two-month extension of time accompanies this submission, extending the time for filing a Notice of Appeal until January 28, 2004. No additional fee is believed to be required for consideration of this response. If any fee is required please charge our Deposit Account Number 19-0733.

hybridizing the amplification product to a first molecular beacon probe which hybridizes to the target nucleic acid and a second molecular beacon probe which hybridizes to the non-target nucleic acid, wherein each of the first and the second molecular beacon probes comprises a photoluminescent dye and a quenching agent at opposite 5' and 3' ends, wherein the photoluminescent dye on the first and second molecular beacon probes are different, and wherein the first molecular beacon probe further comprises a ~~first stem and a loop, wherein the stem~~ **which comprises** about 4 base pairs having a sequence 5'-CACG-3', and a ~~first the loop structure which~~ **comprises** about 16 base pairs and has a  $T_m$  of about 50-51°C; and

detecting the first and the second molecular beacon probes hybridized to the target nucleic acid, thereby detecting the target nucleic acid.

68-99. (Canceled)

100. (Currently Amended) The method of claim 65, 66, or ~~68~~ 67, wherein the second molecular beacon probe comprises a ~~second stem and a second loop structure~~, wherein the ~~second loop~~ comprises about 19-20 base pairs and has a  $T_m$  of about 54-56°C, and wherein the ~~second stem~~ comprises about 4 base pairs having a sequence 5'-CACG-3'.

101. (Currently Amended) The method of claim 100, wherein the ~~second loop of the second molecular beacon probe~~ consists of 19-20 base pairs and has a  $T_m$  of 54-56°C, and wherein the ~~second stem of the second molecular beacon probe~~ consists of 4 base pairs having a sequence 5'-CACG-3'.

102-109. (Canceled)

110. (Currently Amended) A method for detecting a target nucleic acid, the method

comprising the steps of:

separating a sample in which a target nucleic acid is present in an amount less than about 20% relative to non-target nucleic acid in said sample, to form a plurality of assay samples;

amplifying said target nucleic acid in said assay samples;

hybridizing the amplification products to a first molecular beacon probe which hybridizes to the target nucleic acid and to a second molecular beacon probe which hybridizes to the non-target nucleic acid, wherein each of the first and the second molecular beacon probes comprises a photoluminescent dye and a quenching agent at opposite 5' and 3' ends, wherein the photoluminescent dye on the first and second molecular beacon probes are different, and wherein the second molecular beacon probe further comprises a ~~second stem and a loop, wherein the stem which comprises~~ about 4 base pairs having a sequence 5'-CACG-3', and ~~a second the loop structure which comprises~~ about 19-20 base pairs and has a  $T_m$  of about 54-56°C; and

detecting the first and the second molecular beacon probes hybridized to the target nucleic acid, thereby detecting the target nucleic acid.

111. (Currently Amended) A method for detecting a target nucleic acid, the method comprising the steps of:

providing a sample comprising X% of a target nucleic acid, wherein X is less than 100;

dividing the sample to produce a plurality of assay samples;

wherein the ratio of target to non-target nucleic acid in at least one of the samples is greater than X%;

amplifying the target nucleic acid to form an amplification product;

hybridizing the amplification products to a first molecular beacon probe which hybridizes to the target nucleic acid and a second molecular beacon probe which hybridizes to the non-target nucleic acid, wherein each of the first and the second molecular probes comprises a photoluminescent dye and a quenching agent at opposite 5' and 3' ends, wherein the photoluminescent dye on the first and second molecular beacon probes are different, and wherein the second molecular beacon probe further comprises a ~~second~~ stem and a loop, wherein the stem ~~comprising~~ **comprises** about 4 base pairs having a sequence 5'-CACG-3', and a ~~second~~ the loop structure ~~comprising~~ **comprises** about 19-20 base pairs and a  $T_m$  of about 54-56°C; and

detecting the first and second molecular beacon probes hybridized to the target nucleic acid, thereby detecting the target nucleic acid.

112. (Currently Amended) A method for detecting a target nucleic acid in a population of non-target nucleic acid contained in a sample, the method comprising:

dividing a heterogenous sample comprising target nucleic acid and non-target nucleic acid to form a plurality of assay samples, wherein the concentration of non-target nucleic acid is at least 5 fold that of target nucleic acid in the heterogeneous sample, and wherein at least one of the assay samples comprises a single molecule of the target nucleic acid;

amplifying the single molecule of target nucleic acid to form an amplification product;

hybridizing the amplification products to a first molecular beacon probe which hybridizes to the target nucleic acid and a second molecular beacon probe which hybridizes

to the non-target nucleic acid, wherein each of the first and the second molecular probes comprises a photoluminescent dye and a quenching agent at opposite 5' and 3' ends, wherein the photoluminescent dye on the first and second molecular beacon probes are different, and wherein the second molecular beacon probe further comprises a ~~second~~ stem and a loop, wherein the stem comprises ~~comprising~~ about 4 base pairs having a sequence 5'-CACG-3', and ~~a second the loop structure comprising~~ comprises about 19-20 base pairs and a  $T_m$  of about 54-56°C; and

detecting the first and second molecular beacon probes hybridized to the target nucleic acid, thereby detecting the target nucleic acid.

113. (Cancelled).

114. (Cancelled).

115. (Currently Amended) The method of claim 65, 66, or 67, wherein the ~~first~~ loop **consists** of 16 base pairs and has a  $T_m$  of 50-51°C, and wherein the ~~first~~ stem **consists** of 4 base pairs having a sequence 5'-CACG-3'.

116. (Currently Amended) The method of claim 110, 111, or 112, wherein the ~~second~~ loop consists of 19-20 base pairs and has a  $T_m$  of 54-56°C, and wherein the ~~second~~ stem consists of 4 base pairs having a sequence 5'-CACG-3'.

117. (New) The method of claim 66 or 111, wherein X is less than 20.

118. (New) The method of claim 65, 66, 67, 110, 111, or 112, wherein the target nucleic acid is a mutant nucleic acid.

119. (New) The method of claim 65, 67, 110, or 112, wherein the non-target nucleic acid is